Notice of Allowability	Application No.	Applicant(s)	
	09/889,516	FAULL ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 4/8/2004*.

2. ☒ The allowed claim(s) is/are *1,3-6 and 8-10 (now renumbered as claims 1-8)*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 1/7/2004
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David Halstead on 6/22/2004.

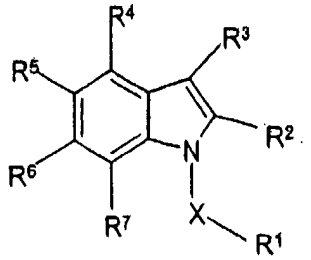
A. The restriction requirement at paper no. 14 is modified so that the elected group I invention is modified to be drawn to the compound of formula I wherein X is CH2 or SO2, R2 is all moieties claimed in the claim amendment filed 4/8/2004 excluding tetrazol-5-yl or the group of formula VI, R3 is as claimed in the claim amendment filed 4/8/2004, R4-R18 and r are all the moieties claimed in the claim amendment filed 4/8/2004, the method of preparing the compounds and using the compounds to treating inflammatory diseases. This restriction is made FINAL. The nonelected subject matter is withdrawn from consideration.

B. In claim 1, line 1, page 2 of the claims filed 4/8/2004, the phrase "inflammatory disease" is amended to "rheumatoid arthritis, glomerular nephritides, lung fibrosis, restenosis, asthma, atherosclerosis, psoriasis, delayed-type hypersensitivity reactions of the skin, inflammatory bowel disease, multiple sclerosis, inflammation resulting from brain trauma, stroke, ischemia, myocardial infarction and transplant rejection".

C. In claim 1, line 6, page 2 of the amendment filed 4/8/2004, the phrase "salt, amide or ester thereof" is amended to –salt or ester thereof"--.

D. In claim 1, lines 8-9, page 3 of the amendment filed 4/8/2004, the phrase "or an amide derivative thereof" is deleted.

E. In claim 9, page 4 of the amendment filed 4/8/2004, line 1, the phrase "A compound of formula (I) as defined in claim 1" is amended to "A compound of formula (I)



(I)

or a pharmaceutically acceptable salt or ester thereof; wherein

X is CH_2 or SO_2;

R^1 is an optionally substituted aryl ring;

R^2 is carboxy, cyano, $-C(O)CH_2OH$, $-CONHR^8$, $-SO_2NHR^9$, SO_3H,

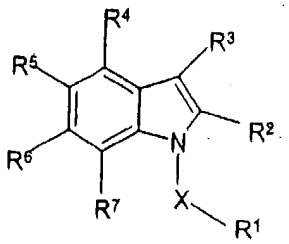
where R^8 is selected from hydrogen, alkyl, aryl, cyano, hydroxy, $-SO_2R^{12}$ where R^{12} is alkyl, aryl, or haloalkyl, or R^8 is a group $-(CHR^{13})_r-COOH$ where r is an integer of 1-3 and each R^{13} group is independently selected from hydrogen or alkyl; R^9 is hydrogen, alkyl, or optionally substituted aryl, or a group COR^{14} where R^{14} is alkyl, aryl, or haloalkyl; and R^{10} and R^{11} are independently selected from hydrogen or alkyl, particularly C_{1-4} alkyl;

R^3 is a group OR^{15}, $S(O)_qR^{15}$, $NHCOR^{16}$, $NHSO_2R^{16}$, $(CH_2)_sCOOH$, $(CH_2)_tCONR^{17}R^{18}$, $NR^{17}R^{18}$, $SO_2NR^{17}R^{18}$ or optionally substituted alkenyl, where q is 0, 1 or 2, s is 0 or an integer of from 1 to 4, t is 0 or an integer of from 1 to 4, R^{15} is a cycloalkyl group or an alkyl group substituted with one or more groups selected from halogen, hydroxy, cyano, amino, mono- or di- alkylamino, C_{1-4} alkoxy, carboxy, sulphonamido, $CONH_2$, morpholino, pyridinyl, pyrimidinyl, phenyl optionally substituted by halogen, carboxy, alkoxy, carbamoyl, acyl groups, or hydroxyalkyl wherein the alkyl group in the hydroxyalkyl moiety includes at least two carbon atoms, R^{16} is optionally substituted alkyl or optionally substituted aryl, and R^{17} and R^{18} are independently selected from hydrogen, optionally substituted alkyl, and optionally substituted aryl, with the proviso that at least one of R^{17} or R^{18} is other than hydrogen; and

R^4 is selected from hydrogen, hydroxyl, halo, alkoxy, aryloxy, araalkyl, carboxyalkyl, or an amide derivative thereof and

R^5, R^6, and R^7 are independently selected from hydrogen, hydroxyl, halo, alkoxy, or an optionally substituted hydrocarbyl group.

F. In claim 10, lines 1-2, page 4 of the amendment filed 4/8/2004, the phrase " A method of preparing a compound of formula (I) as defined in claim 1" is amended to –A method of preparing a compound of formula (I):



(I)

or a pharmaceutically acceptable salt or ester thereof; wherein

X is CH_2 or SO_2;

R^1 is an optionally substituted aryl ring;

R^2 is carboxy, cyano, $-C(O)CH_2OH$, $-CONHR^8$, $-SO_2NHR^9$, SO_3H,

where R^8 is selected from hydrogen, alkyl, aryl, cyano, hydroxy, $-SO_2R^{12}$ where R^{12} is alkyl, aryl, or haloalkyl, or R^8 is a group $-(CHR^{13})_r-COOH$ where r is an integer of 1-3 and each R^{13} group is independently selected from hydrogen or alkyl; R^9 is hydrogen, alkyl, or optionally substituted aryl, or a group COR^{14} where R^{14} is alkyl, aryl, or haloalkyl; and R^{10} and R^{11} are independently selected from hydrogen or alkyl, particularly C_{1-4} alkyl;

R^3 is a group OR^{15}, $S(O)_qR^{15}$, $NHCOR^{16}$, $NHSO_2R^{16}$, $(CH_2)_sCOOH$, $(CH_2)_tCONR^{17}R^{18}$, $NR^{17}R^{18}$, $SO_2NR^{17}R^{18}$ or optionally substituted alkenyl, where q is 0, 1 or 2, s is 0 or an integer of from 1 to 4, t is 0 or an integer of from 1 to 4, R^{15} is a cycloalkyl group or

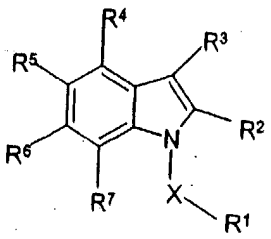
an alkyl group substituted with one or more groups selected from halogen, hydroxy, cyano, amino, mono- or di- alkylamino, C_{1-4} alkoxy, carboxy, sulphonamido, $CONH_2$, morpholino, pyridinyl, pyrimidinyl, phenyl optionally substituted by halogen, carboxy, alkoxy, carbamoyl, acyl groups, or hydroxyalkyl wherein the alkyl group in the hydroxyalkyl moiety includes at least two carbon atoms, R^{16} is optionally substituted alkyl or optionally substituted aryl, and R^{17} and R^{18} are independently selected from hydrogen, optionally substituted alkyl, and optionally substituted aryl, with the proviso that at least one of R^{17} or R^{18} is other than hydrogen; and

R^4 is selected from hydrogen, hydroxyl, halo, alkoxy, aryloxy, araalkyl, carboxyalkyl, or an amide derivative thereof and

R^5, R^6, and R^7 are independently selected from hydrogen, hydroxyl, halo, alkoxy, or an optionally substituted hydrocarbyl group. ---

G. In claim 10, line 2, page 5 of the amendment filed 4/8/2004, the phrase "where R4, R5, R6 and R7 are as defined in claim 1," is deleted.

H. In claim 1, lines 5-7, page 2 of the amendment filed 4/8/2004, the phrase "



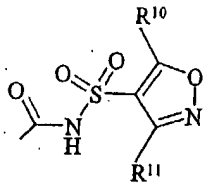
(I)

or a pharmaceutically acceptable salt or ester thereof; wherein

X is CH_2 or SO_2;

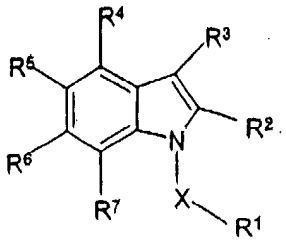
R^1 is an optionally substituted aryl ring;

R^2 is carboxy, cyano, $-C(O)CH_2OH$, $-CONHR^8$, $-SO_2NHR^9$, tetrazol-5-yl, SO_3H, or a group of formula (VI)



(VI)

is amended to ---



(I)

or a pharmaceutically acceptable salt or ester thereof; wherein

X is CH_2 or SO_2;

R^1 is an optionally substituted aryl ring;

R^2 is carboxy, cyano, $-C(O)CH_2OH$, $-CONHR^8$, $-SO_2NHR^9$, or SO_3H, -------.

I. In claim 1, page 3 of the amendment filed 4/8/2004, line 3, the phrase "R^{15} is a substituted alkyl or cycloalkyl group" is amended to --- R^{15} is a substituted cycloalkyl group or an alkyl group substituted with one or more groups selected from halogen, hydroxy, cyano, amino, mono- or di- alkylamino, C_{1-4} alkoxy, carboxy, sulphonamido, $CONH_2$, morpholino, pyridyl, pyrimidinyl, phenyl optionally substituted by halogen, carboxy, alkoxy, carbamoyl, acyl groups, or hydroxyalkyl wherein the alkyl group in the hydroxyalkyl moiety includes at least two carbon atoms.

J. In claim 10, lines 2-3, page 5 of the amendment filed 4/8/2004, the phrase "$R^{2'}$ is a group R^2 as defined in claim 1 or a protected form thereof, and $R^{3'}$ is a group R^3 as defined in claim 1" is amended to --- $R^{2'}$ is a group R^2 or a protected form thereof, and $R^{3'}$ is a group R^3---.

K. In claim 10, line 6, page 5 of the amendment filed 4/8/2004, the phrase "R^1 and X are as defined in claim 1" is amended to ----R^1 is an optionally substituted aryl ring and X is CH_2 or SO_2---.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: The IDS filed 1/7/2004 has been considered and does not read on nor render obvious the claimed subject matter.

The closest prior art reference is Sechra et. al. (See Reference A). The difference between the Sechra anti-inflammatory compound and the instantly claimed anti-inflammatory compound is the R2 group and the R5 group. In the instant compound, the R^2 group is a carboxy and the R5 group is alkoxy. In the Sechra compound, the R^2 group is methyl; the R5 group is benzyloxy. At columns 1-24, see compound, Ethenesulfonamide, N-ethyl-2-[3-[1-phenylmethyl)-4-piperidinyl]-1H-indol-5-yl]-, hydrochloride.

The prior art reference does not teach nor suggest to one of ordinary skill in the art how to modify the prior art compound to derive the instant compound. Therefore, the instant claims are allowable therefrom.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
June 22, 2004

JOSEPH K. McKANE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600